

**University Of Khartoum**  
**Graduate College**  
**Medical & Health Studies Board**

**A CLINICOPATHOLOGICAL STUDY ON  
BREAST CANCER IN SUDANESE PATIENTS**

By

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## **DEDICATION**

To the sole of my father

To the members of my family

With great appreciation.

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## List of Abbreviations

<b>aa</b>	Amino Acid.
<b>ADH</b>	Atypical ductal hyperplasia.
<b>AJCC</b>	American Joint Committee on Cancer.
<b>ALH</b>	Atypical lobular hyperplasia.
<b>BC</b>	Breast cancer.
<b>BCE</b>	Breast clinical examination
<b>BSE</b>	Breast self examination
<b>BRCA -1</b>	A gene involved in pathogenesis of BC.
<b>BRCA- 2</b>	A gene involved in pathogenesis of BC.
<b>CA</b>	Cyclophosphamide, Doxorubicin.
<b>CCC</b>	Colombia Clinical Classification.
<b>CMF</b>	Cyclophosphamide, Methotrexate, and Fluorouridine
<b>DCIS</b>	Ductal carcinoma in situ.
<b>DLU</b>	Ductal lobular unit.
<b>DNA</b>	Deoxyribonucleic acid.
<b>e.g.</b>	For example.
<b>EGFR</b>	Epidermal growth factor receptors.
<b>ER</b>	Estrogen receptors.
<b>IDC</b>	Invasive ductal carcinoma.
<b>H&amp;E</b>	Hematoxylin and Eosine

<b>kd</b>	Kilo Dalton.
<b>LCIS</b>	Lobular carcinoma in situ.
<b>LN</b>	Lymph node.
<b>MALT</b>	Mucosal associated tissue.
<b>ml</b>	Milliliter.
<b>MRI</b>	Magnetic resonant image.
<b>NHL</b>	National Health Laboratory, Sudan.
<b>NOS</b>	Not otherwise specified.
<b>PR</b>	Progesterone receptors.
<b>RICK</b>	Radio-isotopes Centre of Khartoum.
<b>TDLU</b>	Terminal ductal lobular unit.
<b>TNM</b>	Tumor, nodes and metastasis system.
<b>U/S</b>	Ultrasonography.
<b>WHO</b>	World Health Organization.
<b>+ve</b>	Positive.
<b>-ve</b>	Negative.



## ABSTRACT

Breast cancer is one of the most important tumors with high morbidity and mortality rates both in the developed and in the developing countries.

This is a retrospective study conducted on the Sudanese patients with BC during the period from January 2002 to December 2005, at the National Health Laboratory in Khartoum, Sudan.

The study had the objective to review the histopathological patterns of BC, and to show the relationships between the histological types of the tumor and the age, sex, residency distribution in addition to the clinical presentations and the modes of surgical treatment.

The study included 300 patients, 262 were females and 38 were males, with a ratio of about 1: 7. The youngest patient was aged 21 years and the eldest was 77 years old.

This study showed a high proportion of the disease in younger age groups, 37.3% of the patients were below 40 years, with a mean age of  $44.45 \pm 13.7$  years.

The study also pointed to the high proportion of BC patients coming from the Central and Northern regions.

All (100%) of the patients were symptomatic with breast lumps. Skin ulceration, nipple retraction and discharge were seen in (9%), (13%) and (10%) in order.

Microscopical examination of the slides identified eight histological types of BC. These were IDC (87.3%), ILC (3.7%), DCIS(4%), LCIS(1%), papillary carcinoma(2%), tubular carcinoma(0.7%), mucinous carcinoma (0.7%) and malignant phyllodes tumors(0.7%).

The study concluded that Sudanese patients share many pathological and epidemiological features of the developing countries for BC. These include earlier age of onset, higher male- female ratio and increased frequency of poor clinical and pathological prognostic indicators.

We emphasis the importance of patients' education and promotion of BC screening program in improving the ultimate outcome of this disease.



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## INTRODUCTION & LITRATURE REVIEW

Breast cancer (BC) is one of the most common human neoplasms, accounting for approximately one third of all cancers in females.<sup>(1)</sup> It is associated with the western lifestyle, so has higher incidence in North America, Europe and Australia.<sup>(2)</sup> In Africa it is the second most common malignancy in females after the carcinoma of the cervix.<sup>(3)</sup> As a cause of cancer death it ranks second after the lung cancer.<sup>(5)</sup>

In Sudan, according to reports derived from the department of medical statistics and registration of NHC and RICK, breast cancer is estimated to account for 33.8% of all cancer cases.<sup>(4)</sup>

Most of the breast cancers are invasive and the majorities (70%-80%) are adenocarcioma, arising from the ductal lobular units of the breast<sup>(6)</sup> About (40%-70%) being invasive ductal carcinoma<sup>(7)</sup>, followed by invasive lobular carcinoma (5%-15%)<sup>(8,9,10)</sup> and tubular carcinoma (2%-7%).<sup>(11)</sup> Rare forms include medullary carcinoma (1%-5%), mucinous (2%), neuroendocrine (1%-2%) and invasive papillary carcinoma (1%).<sup>(12)</sup> In addition are the non epithelial malignant tumors as malignant lymphoma, mesenchymal and metastatic tumors.<sup>(13, 14,15)</sup>



Breast cancer is rare before the age of 25 years, its peak age at the time of diagnosis is 58 years.<sup>(5)</sup> Male breast cancer is extremely rare; the male: female ratio being 1-2:100. This ratio is reported higher in African and black populations.<sup>(16,17)</sup>

Breast cancer is recognized as having familial tendency.<sup>(18)</sup> Genes implicated include BRCA 1 and BRCA 2 genes mutations.<sup>(19,20)</sup> Hormonal, nutritional and other environmental factors are also established etiological factors.<sup>(21,22,23,24)</sup> High risk precursor lesions of invasive cancer include ductal carcinoma in situ<sup>(25,26)</sup> fibrocystic disease with atypical ductal hyperplasia<sup>(27,28)</sup> and lobular carcinoma in situ<sup>(29,30)</sup>. While low risk lesions include benign myoepithelial and fibroepithelial lesions as fibroadenoma.<sup>(31)</sup>

Breast cancer is diagnosed and screened basing on the triple assessment (clinical, radiological and pathological), while surgical and adjuvant medical modalities are tried to manage this disease.<sup>(119)</sup>

## 1.1 Normal anatomy and histology of the breast:

### 1.1.1 Gross anatomy:

Breast, or mammary gland, is a modified apocrine sweat gland lying in the anterior chest wall. It extends from the second to the sixth rib, lying on the superficial fascia of the chest wall, with a

small axillary tail extending upwards and laterally into the deep fascia<sup>(33)</sup> After puberty in females, the breast enlarges and takes its spherical shape with a central nipple surrounded by colored areola.<sup>(32)</sup> The breast consists fifteen to twenty lobes radiating from the nipple.<sup>(33)</sup>

#### 1.1.2 Blood supply and lymphatic draining:

Arterial blood supply to the breast is from the perforating branches of the internal thoracic artery and the intercostal arteries, the axillary artery also supplies the breast via its lateral thoracic and thoracoacromial branches. The veins correspond to the arteries.<sup>(34)</sup>

The lymphatic draining of the mammary glands is very important clinically because it is related to cancer spread, then staging and prognosis.<sup>(35)</sup> The lateral quadrants of the breast drain into the anterior axillary or pectoral lymph nodes. The medial quadrants drain by means of vessels that pierce the intercostal space and enter the internal thoracic lymph nodes within the thorax. Some vessels drain in the posterior intercostal nodes; while some may communicate with the opposite breast.<sup>(36)</sup>

#### 1.1.3 Normal histology:

The functional unit of the breast is the ductal lobular unit (DLU).<sup>(37)</sup> Composed of acini, interlobular stroma and intralobular

ducts which bud from subsegmental ducts that drain into segmental ducts. The segmental ducts with their branches and interlobular stroma and fatty tissue form a lobe. The ducts are lined by two layers of epithelium; an inner cuboidal or columnar and outer discontinuous layer of contractile myoepithelial cells. The epithelium is invested in continuous basement membrane.<sup>(37)</sup> Most of the interlobular stroma consists of dense fibrous tissue admixed with adipose tissue. The intralobular stroma is delicate myxomatous tissue containing scanty lymphocytes.<sup>(37)</sup>

## 1.2 Breast pathology:

### 1.2.1 Congenital anomalies:

All are very rare and impose no diagnostic difficulties.

They include: -<sup>(72)</sup>

- Supernumerary nipples or breasts.
- Accessory axillary breast tissue.
- Congenital inversion of nipples.
- Juvenile hypertrophy (Macromastia)

### 1.2.2 Inflammatory conditions:

Are rare but can mimic breast cancer both clinically and histologically.<sup>(73)</sup> They include:-

- Acute mastitis: present as painful mass, usually during lactation.

- Tuberculous mastitis: shows typical granuloma. Clinically may mimic advanced cancer.<sup>(74)</sup>
- Periareolar mastitis (Zuska's disease): is a periareolar abscess associated with squamous metaplasia of the lactiferous ducts.<sup>(75)</sup>
- Mammary duct ectasia: Is dilatation of the large ducts with accumulation of fatty depresses, calcification and florid inflammatory reaction with no epithelial hyperplasia. May mimic BC by causing nipple retraction.<sup>(76)</sup>
- Fat necrosis: Characterized by foamy macrophages infiltrating necrotic adipose tissue and dense inflammatory cells infiltration. Like cancer, can cause solid mass and skin retraction.<sup>(77)</sup>
- Lymphocytic mastopathy: characterized by dense peri and intralobular lymphocytic infiltration associated with lobular atrophy and sclerosis. Usually mistaken as breast lymphoma.<sup>(78)</sup>
- Granulomatous lobular mastitis: characterized by non caseating granuloma confined to one lobule.<sup>(79)</sup>

### 1.2.3 Benign epithelial lesions:

- Non proliferative breast changes (fibrocystic changes) present clinically as breast lumps mimicking carcinoma. Morphological changes include cyst formation often with apocrine metaplasia, fibrosis and adenosis.<sup>(80)</sup>

- Proliferative breast diseases without atypia. These lesions include:

A) Simple epithelial hyperplasia: Characterized by proliferation of the ductal epithelium to more than two cell layers without cellular abnormalities.<sup>(81)</sup>

B) Sclerosing adenosis: denotes marked increased in the number of the acini with their compression in the central part of the lesion with calcification, mimicking the invasive carcinoma.<sup>(82)</sup>

C) Radial scar is a stellated lesion characterized by a nidus of glands in hyalinized stroma. This condition can simulate breast cancer both in morphology and in mammography.<sup>(83)</sup>

- Proliferative breast diseases with atypia:

A) Atypical ductal hyperplasia (ADH): characterized by epithelial proliferation with incompletely monomorphic cell population, regular cell placement and round lumen, markedly simulating the DCIS with some quantitative and qualitative differences.<sup>(84)</sup>

B) Atypical lobular hyperplasia (ALH): show monomorphic small rounded loosely cohesive cells, partially filling the lobules with less than 50% of the acini is fully distended, quantitative difference from the LCIS.<sup>(47)</sup>

#### 1.2.4 Breast tumors:

### **(WHO histological classification of breast tumors) (Appendix 2)**

#### **I. Epithelial tumors:**

##### 1.1 Invasive ductal carcinoma, not otherwise specified (NOS).

1.1.1 Mixed type carcinoma.

1.1.2 Pleomorphic carcinoma.

1.1.3 Carcinoma with osteoclastic giant cells.

1.1.4 Carcinoma with chondrocarcinomatous feature.

1.1.5 Carcinoma with melanotic feature.

##### 1.2 Invasive lobular carcinoma.

##### 1.3 Tubular carcinoma.

##### 1.4 Invasive cribriform carcinoma.

##### 1.5 Medullary carcinoma.

##### 1.7 Mucinous carcinoma and other tumors with abundant mucin

1.7.1 Mucinous carcinoma.

1.7.2 Cystadenocarcinoma and columnar cell mucinous carcinoma.

1.7.3 Signet ring cell carcinoma.

##### 1.8 Neuroendocrine tumors.

1.8.1 Solid neuroendocrine tumors.

1.8.2 Atypical carcinoid tumors.

1.8.3 Small cell / oat cell tumors.

- 1.8.4 Large cell neuroendocrine carcinoma.
- 1.9 Invasive papillary carcinoma.
- 1.10 Apocrine carcinoma.
- 1.11 Metaplastic carcinoma.
  - 1.11.1 Pure epithelial metaplastic carcinoma.
    - 1.11.1.1 Squamous cell carcinoma.
    - 1.11.1.2 Adenosquamous carcinoma with spindle cell metaplasia.
    - 1.11.1.3 Adenosquamous carcinoma.
    - 1.11.1.4 Mucoepidermoid carcinoma.
  - 1.11.2 Mixed epithelial cell / mesenchymal tumors.
- 1.12 Lipid rich carcinoma.
- 1.13 Secretory carcinoma.
- 1.14 Oncocytic carcinoma.
- 1.15 Adenoid cystic carcinoma.
- 1.16 Acinic cell carcinoma.
- 1.17 Glycogen-rich clear cell carcinoma.
- 1.18 Sebaceous carcinoma.
- 1.19 Inflammatory carcinoma.
- 1.20 Lobular neoplasia.
  - 1.20.1 Lobular carcinoma in situ.
- 1.21 Intralobular proliferative lesions.

- 1.21.1 Usual ductal hyperplasia.
- 1.21.2 Flat epithelial atypia.
- 1.21.3 Atypical ductal hyperplasia.
- 1.21.4 Ductal carcinoma in situ.
- 1.22 Microinvasive carcinoma.
- 1.23 Intraductal papillary neoplasia.
  - 1.23.1 Central papilloma.
  - 1.23.2 Peripheral papilloma.
  - 1.23.3 Atypical papilloma.
  - 1.23.4 Intraductal papillary carcinoma.
  - 1.23.5 Intracystic papillary carcinoma.
- 1.24 Benign epithelial proliferations.
  - 1.24.1 Adenosis including variants.
    - 1.24.1.1 Sclerosing adenosis.
    - 1.24.1.2 Apocrine adenosis.
    - 1.24.1.3 Blunt ducts adenosis.
    - 1.24.1.4 Microglandular adenosis.
    - 1.24 1.5 Adenomyoepithelial adenosis.
  - 1.24.2 Radial scar / complex sclerosing lesions.
  - 1.24.3 Adenomas.
    - 1.24.3.1 Tubular adenoma.
    - 1.24.3.2 Lactating adenoma.



1.24.3.3 Apocrine adenoma.

1.24.3.4 Pleomorphic adenoma.

1.24.3.5 Ductal adenoma.

## **2. Myoepithelial lesions**

2.1 Adenomyoepithelial adenosis.

2.2 Adenomyoepithelioma.

2.3 Malignant myoepithelioma.

## **3. Mesenchymal tumors**

3.1 Haemangioma.

3.2 Haemangiopericytoma.

3.3 Psedoangiomatous stroma hyperplasia.

3.4 Myofibroblastoma.

3.5 Fibromatosis.

3.6 Inflammatory myofibroblastic tumors.

3.7 Lipoma.

3.8 Angiolipoma.

3.9 Granular cell tumors.

3.10 Neurofibroma.

3.11 Schwannoma.

3.12 Angiosarcoma.

3.13 Liposarcoma.

3.14 Rhabdomyosarcoma.

3.15 Osteosarcoma.

3.16 leiomyoma.

3.17 Leiomyosarcoma.

#### **4. Fibroepithelial tumor**

4.1 Fibroadenoma

4.2 Phylloides tumors

4.2.1 Benign

4.2.2 Borderline

4.2.3 Malignant

4.3 Periductal stromal sarcoma, low grade

4.4 Mammary hamartoma

#### **5. Tumors of the nipple**

5.1 Nipple adenoma

5.2 Syringiomatous adenoma

5.3 Paget's disease of the nipple

#### **6. Malignant lymphoma**

6.1 Diffuse large B-cell lymphoma

6.2 Burkett's lymphoma

6.3 Extra nodal B-cell lymphoma of MALT type

6.4 Follicular lymphoma

#### **7. Metastatic tumors.**

#### **8. Tumors of the male breast.**

## 8.1 Gynaecomastia

## 8.2 Carcinoma

### 8.2.2 Invasive

### 8.2.2 In situ

## 1.3 Epidemiology and risk factors of breast cancer:

### 1.3.1 Epidemiology:

Breast cancer is the most common non skin malignant tumor and the leading cause of cancer death in women, with more than 1000.000 cases occurring world wide annually.<sup>(39)</sup> In United States, it was reported that each year approximately 100.000 new cases are diagnosed and around 30.000 die from the disease.<sup>(40)</sup> The life time risk is about 13% for females and around 0.11%for males.<sup>(41)</sup> The incidence is high in America and North Europe (about 9.4 new cases pre 100.000 women each year).<sup>(41)</sup> In America the detection and then incidence of BC increased due to wide spread of mammography.<sup>(39)</sup> Intermediate incidence is seen in Southern European and Latin American countries. The incidence of BC is relatively low in African and Asian countries. However, it is second most common malignancy in an African female population after cervical cancer.<sup>(42)</sup>

In Sudan, breast cancer is the most common malignant tumor in females .It is the leading cause of cancer mortality among the Sudanese females.<sup>(4)</sup>

#### 1.3.2. Risk factors:-

Proved risk factors of BC include familial & genetic, hormonal and environmental factors.<sup>(40,43)</sup> It has been proposed that the common dominator for these risk factors is strong and/or prolonged estrogen stimulation operating on susceptible genetic back ground.<sup>(43)</sup>

**1- Age:** 75% of breast cancer occurs after the age of 50 years.<sup>(44)</sup>

The mean age for breast cancer in some Arab and African countries was found 48.3 years.<sup>(42)</sup>

**2- Age at menarche:** less than 11 years has 20% increased risk.<sup>(45)</sup>

**3- Parity:** women with first full pregnancy at age younger than 20 years have half risk of nulliparous and older women.<sup>(45)</sup>

**4- Family history:** positive family history is found in 13% of women with BC.<sup>(46)</sup> Some studies found that women who have first degree relatives with BC have increased risk by two to three times to develop the disease.<sup>(46)</sup>

**5- Breast biopsy:** risk increases by 4-5 times with prior breast biopsies showing atypical ductal or lobular hyperplasia.<sup>(47)</sup>

**6- Race:** the risk of developing BC in next 20 years at the age of 50 years is 1 in 15 in Caucasian, 1 in 20 in African American, 1 in 25 in Asian/Pacific Islanders and 1 in 27 in Hispanics. <sup>(48)</sup>

**7 - Estrogen exposure:** decrease in endogenous estrogen reduces the risk by up to 75 %. <sup>(49)</sup> While many studies regarding oral contraceptive use show no increase risk to BC. <sup>(50, 51)</sup>

**8- Radiation exposure:** therapeutic radiation for lymphoma increase the risk by 20%- 30 %. <sup>(52)</sup>

Other recognized but difficult to quantify factors include:

1- Breast feeding some studies pointed that breast feeding reduces the risk of breast cancer. <sup>(53)</sup>

2- Geographical influence.

3- Diet and alcohol. <sup>(44)</sup>

4- Environmental toxins.

5- Tobacco. <sup>(43)</sup>

6- Obesity and anthropometric indices.

7- Exercise. <sup>(43)</sup>

## 1.4 Genetics and Pathogenesis:

Breast cancer has multifactorial aetiology involving genetic, environmental and hormonal factors. <sup>(54)</sup>

**Familial breast cancer** is related to genetic alterations including inactivation of oncosuppressor genes or over expression of oncogenes .Well studied are BRCA-1 and BRCA-2 genes mutations.<sup>(55)</sup>

**BRCA-1 gene** is an 81 kb oncosuppressor gene located at the long arm of the chromosome 17(17q21).<sup>(56)</sup> BRCA-1 protein is an 1863 amino acids phosphoprotien. It functions in transcriptional regulation, cell cycle control and chromatin remodeling.<sup>(57)</sup> It protects the cell from damage by stopping cell cycle.BRCA-1 gene mutation carries life time risk for BC of 60% to 80%.<sup>(58)</sup> Histological patterns of BC associated with BRCA-1 mutations include medullary carcinoma and ER –PR and Her 2/ neu negative carcinomas. Other cancers include ovarian, prostatic, and colorectal cancers.<sup>(55)</sup>

**BRCA-2:** is an 84 kd gene located at the long arm of the chromosome 13(13p12.2).<sup>(59)</sup> BRCA-2 protein is a 3418 polypeptide. It act as DNA repairing factor by binding to BRCA-1 to form a nuclear dot complex at the site of DNA repair.<sup>(60)</sup> Mutation carries 60% to 80% risk for BC, with higher association with male breast cancer.<sup>(61)</sup>

**Her-2 neu gene:** is an oncogene that encodes a transmembrane glycoprotein with tyrosine kinase activity known as p185, which belongs to the family of EGFR genes. HER-2/neu is a

very good predictor of response to Herceptin, but not to chemotherapy or overall survival. It is found in nearly all cases of high grade (comedo-type) DCIS, in 20-30% of IDC, and in a smaller percent of ILC.<sup>(62)</sup>

**Other genes:** Genes other than BRCA-1 and BRAC-2 involved in BC susceptibility include the check point kinetic gene CHEK2;<sup>(63,64)</sup> as well as the oncosuppressor genes p53, PTEN and LKBI/STKII .<sup>(65)</sup> While oncogenes include ER, EGFR, RAS, CCND-1 and other genes.<sup>(63)</sup>

**Sporadic breast cancers** are related more to environmental and hormonal factors.<sup>(41)</sup> Estrogen excess hypothesis stipulates that BC risk depend on direct exposure to estrogen.<sup>(66)</sup> It is said to give metabolites that cause mutations or generate DNA damaging free radicals.<sup>(67)</sup> Hormonal action of estrogen also can drive proliferation of cancer cells.<sup>(67)</sup> Estrogen plus progesterone hypothesis highlights the role of progesterone in enhancing the action of estrogen.<sup>(68, 69)</sup>

## 1.5 Localization of breast cancer:

Carcinomas arise from the mammary epithelium and most frequently from the TDLU. Studies reported slightly higher frequency of BC in the left breast with left to right ratio 1.07 to 1.00.<sup>(70, 71)</sup>

Location of the breast cancer is usually indicated in relation to the breast quadrants. 50% are in the upper outer quadrant, 15% in the upper inner quadrant, and 10% in the lower outer quadrant, 5% in the lower inner quadrant, 7% in the central region and 3% are multicentric lesions.

Bilateral breast cancer is detected in less than 5% of patients. A higher percentage being of lobular type.<sup>(71)</sup>

## 1.6 Metastasis and spread of breast cancer:

Breast cancer may spread via lymphatic and hematogenous routes and by direct extension to the adjacent anatomical structures.

<sup>(85)</sup> Spread via the lymphatic route is most frequently to the ipsilateral axillary lymph nodes, internal mammary nodes and other regional nodes groups. Most common sites for distant metastasis are bone, lung and liver. Unusual sites for metastasis include peritoneal surface, gastrointestinal tract and reproductive organs.<sup>(86)</sup>

## 1-7 Diagnosis and screening:

Breast cancer is best diagnosed by the triple assessment including clinical examination, mammography and pathological studies.



### 1-7-1 Clinical pictures of breast cancer:

The majority of breast cancers present symptomatically, but introduction of breast screening has led to increasing proportion of asymptomatic cases.<sup>(87)</sup> Clinical signs and symptoms of breast cancer include pain (mastalgia), palpable mass or lumpiness, nipple discharge and changes, skin changes and others.<sup>(87)</sup> Pain is present in 10% of breast cancer cases, although the majority of the painful conditions are benign. Comes second is the palpable mass. The frequency of the malignant masses depends on the age, only 10% of breast masses in women under the age of 40 years prove malignant compared to 60% in women over 50% years.<sup>(87)</sup> Nipple discharge is more indicative of breast cancer in older women and when it is spontaneous and unilateral.<sup>(87)</sup> Skin changes include peau d'orange and ulcerations. Other clinical features of breast cancer include upper limb oedema and systemic features of malignancy.<sup>(88,89)</sup>

### 1-7-2 Screening of breast cancer:-

Screening denotes detection of the disease before appearance of its signs and symptoms.<sup>(90)</sup> Breast cancer screening program, first introduced in early 1980s, aims at reduction of mortality by discovering preclinical breast cancer in asymptomatic

patients.<sup>(90)</sup> It is especially recommended in high risk population including women over 40 years and women with strong familial tendency.<sup>(91)</sup> It is estimated that screening of average risk population can reduce the mortality by up to 25 %.<sup>(92)</sup> Clinical screening includes breast self examination (BSE) and clinical breast examination (CBE) of the breast tissue and axilla to detect any palpable mass or LN.<sup>(93)</sup> Screening mammography is especially recommended for women over 40 years. Finding in mammography include densities and calcifications.<sup>(94)</sup>

#### 1-7-3 Diagnostic studies:

Histological examination of tissue biopsy is still the gold stander in diagnosis of breast cancer.<sup>(95)</sup> Useful diagnostic tools include fine needle aspiration (FNA) cytology, and imaging .Ancillary studies include immunohistochemical, cytogenetic and molecular biology techniques.<sup>(95)</sup>

Tissue biopsy is either obtained surgically (incisional or excisional) or by core needle biopsy technique, stained with H&E stain with or without other especial stains.<sup>(95)</sup>

Fine needle aspiration is cheap and easy to perform, with up to 90% diagnostic accuracy rate.<sup>(96)</sup> Its sensitivity is up to 84%.

Diagnostic mammography is performed to clarify breast abnormalities and to give additional information about other areas of involvement.<sup>(97)</sup> Other imaging methods include:

1- Digital mammogram.

2- Breast ultrasonography (U/S) and magnetic resonant imaging (MRI).

3- Thermography of the breast.

4- Computed tomography scan (CT-Scan) and positron emission tomography scan (PET- scan)<sup>(97)</sup>.

## 1-8 Pathology of the breast cancer

### 1-8-1Gross Pathology:

Most breast cancers are firm to hard moderately defined masses, in variable sizes. In later stages they can form exophytic or fungating masses with skin ulcerations. In cross section whitish to yellow tissue with areas of necrosis are seen, together with small pinpoint or streaks of white chalky elastotic stroma.<sup>(98)</sup>

### 1-8-2 Histological Types of Breast cancer (Appendix 2)

Almost all of the breast cancer are adenocarcinoma, arising from terminal ductal lobular unit (TDLU).<sup>(99)</sup> Other malignancies account for less 3%, including squamous cell carcinoma,

lymphomas, malignant phyllodes tumors, and other mesenchymal tumors.<sup>(100)</sup>

Summarized WHO histological classification of Breast Cancer:

1. Noninvasive:

- a. Ductal carcinoma in situ.
- b. Lobular carcinoma in situ.

2. Invasive:

- a. Invasive ductal carcinoma.
- b. Invasive ductal carcinoma with a predominant intraductal component.
- c. Invasive lobular carcinoma.
- d. Mucinous carcinoma.
- e. Medullary carcinoma.
- f. Papillary carcinoma.
- g. Tubular carcinoma.
- h. Adenoid cystic carcinoma.
- i. Secretory (juvenile) carcinoma.
- j. Apocrine carcinoma.
- k. Carcinoma with metaplasia.
  - i. Squamous type.

ii. Spindle-cell type.

iii. Cartilaginous and osseous type.

iv. Mixed type.

I. Others.

3. Paget's disease of the nipple.

Non invasive carcinoma (Carcinoma in situ):

- **Ductal carcinoma in situ (DCIS):** Account for 15% to 20% of all breast cancer where mammography is widely used. <sup>(101)</sup> Histologically it is characterized by variable cellular atypia without stromal invasion.<sup>(102)</sup> Architectural patterns of DCIS include comedocarcinoma, solid, cribriform, papillary and micropapillary types.<sup>(102)</sup>
- **Lobular carcinoma in situ (LCIS):** Represents less than 2% of cancer cases.<sup>(103)</sup> Characterized by intralobular proliferation of loosely cohesive cells, with no basement membrane penetration or stromal invasion. 40% to 50% of LCIS are bilateral. <sup>(104)</sup>

Invasive carcinomas:

- **Invasive ductal carcinoma (IDC):** Comprises about 70% to 90% of breast cancer cases. Histologically the tumor cells are arranged in cords, nests and trabeculae, or solid syncytial pattern with minimal stroma. <sup>(105)</sup> Most cases have no specific architecture and assigned as IDC not otherwise specified (NOS). Other may take

comedo, papillary, cribriform and other patterns seen in DCIS, all are characterized by stromal invasion.<sup>(105)</sup>

- **Invasive lobular carcinoma (ILC):** Represents about 5% of cases, in histological section, this tumor appear composed of in cohesive small round cells disperse through fibrous connective tissue, arranged in single files linear cords invading the stroma. Other patterns include solid, alveolar and pleomorphic lobular carcinoma.<sup>(106)</sup>
- **Tubular Carcinoma:** Composed of single layered open tubules with oval or rounded edges.<sup>(107)</sup>
- **Medullary carcinoma:** By definition, this type has syncytial architecture, no tubular or glandular structure and diffuse lymphoplasmacytic stroma infiltration. The cells are usually round with abundant cytoplasm and vesicular nuclei.<sup>(108)</sup>
- **Mucinous carcinoma:** Characterized by proliferating clusters of small cell floating in lakes of mucin.<sup>(109)</sup>
- **Invasive Papillary carcinoma:** Histological sections in this type show delicate or blunt papillae with focal solid area. Cells typically show amphophilic cytoplasm and moderately pleomorphic nuclei.<sup>(110)</sup>
- **Metaplastic carcinomas:** Are heterogeneous group of tumor characterized by presence of admixture of adenocarcinoma with

dominant areas of spindle cells, squamous and/or mesenchymal differentiation.

- **Paget's disease of the nipple:** Represents less than 2% of the cases. It is extension of malignant cells from DCIS into nipple skin without crossing the basement membrane. The tumor (Pagetoid) cells are large and easily detected. <sup>(111)</sup>
- **Carcinoma of male breast:** Breast cancer is very rare in males with male: female ratio less than 1:100 worldwide.<sup>(40)</sup> But higher ratio is observed in Africa.<sup>(42)</sup> However, pathological feature of male breast cancer is similar to that in female, although papillary carcinoma is more common.<sup>(112)</sup>
- **Malignant phyllodes tumors:** Characterized by intracanalicular growth pattern with leaf-like projection into dilated ducts. It consists of epithelial and myoepithelial component and sarcomatous stroma with heterogeneous differentiation.

## 1-9 Staging of breast cancer:

Tumor staging is a numerical description of the degree of invasion and metastatic spread of the tumor. Staging of breast cancer is valuable both in treatment choice and as a prognostic factor. <sup>(113)</sup>

The **TNM** classification devised by the International Union Against Cancer (UICC) and accepted by the American Joint Commission on Cancer (AJCC) is a world standard.<sup>(113)</sup> It is the most accurate but too cumbersome and complicated. The TNM is based on the clinical features of tumor (T), the regional lymph nodes (N), and the presence or absence of distant metastases (M).<sup>(114)</sup>

**\* AJCC stage groupings of breast cancer, based on TNM score<sup>(113)</sup>**

**(Appendix 3)**

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage IIA	T0, N1, M0
	T1, N1, M0
	T2, N0, M0
Stage IIB	T2, N1, M0
	T3, N0, M0
Stage IIIA	T0, N2, M0
	T1, N2, M0
	T2, N2, M0
	T3, N1, M0
	T3, N2, M0



Stage IIIB

T4, Any N, M0

Any T, N3, M0

Stage IV

Any T, Any N, M1

Other staging systems for breast cancer include Manchester and the Columbia Clinical Classification (CCC).<sup>(113)</sup> In the latter system, stage A represents a tumor confined to the breast; stage B include tumors with clinical axillary lymph node enlargement; stage C represents the presence of grave prognostic signs in the breast, stage D indicates metastatic disease.

## 1-10 Grading of breast cancer:

Tumor grading is numerical expression of the degree of its cellular differentiation.<sup>(115)</sup> It is based on careful assessment of histological section under the microscope. Studies showed significant association between the histological grades in invasive cancer and the prognosis.<sup>(116)</sup> So it should be included in minimal data set in reporting breast cancer. Currently used grading system is Modified Bloom's and Richardson's system.<sup>(118)</sup> Other types include Elliston and Ellis, Pately and Craft systems.

**Modified Bloom's and Richardson's System:** Is based on three histological parameters; tubular formation, degree of nuclear

pleomorphism and mitotic count.<sup>(118)</sup> All are estimated under high power field (X40); using standard microscope (e.g. Nikon Lab Photo with field diameter .59 mm and field area 274mm<sup>2</sup>). Scoring:

Tubular formation: 1 – 3 points

Nuclear pleomorphism: 1 – 3 points

Mitotic count: 1 – 3 points

Final grading classification is obtained by summation of these scores:-

Grade I (well differentiated): 3 – 5 points

Grade II (moderately differentiated) 6 – 7 points

Grade III (poorly differentiated): 8 – 9 points

## 1-11 Treatment of breast cancer:

The main types of treatments for breast cancer are surgery, radiation, chemotherapy and hormonal therapy.<sup>(119)</sup> Recent advances in this field include introduction of immunotherapy and gene-targeted therapy.<sup>(119)</sup> Selection of type of treatment is influenced by the age of the patient, the clinical stage of the disease (node +ve and node –ve Tumors), pathological characteristics and the level of estrogen and progesterone receptors. <sup>(120)</sup>

#### 1-11-1 Surgical treatment (types of operation):

- 1- Modified radical mastectomy: denotes removal of the whole breast tissue plus axillary fat, fascia and lymph nodes.
- 2- Quadrantectomy: is the removal of entire segment of the breast which contains the tumor. This is usually accompanied with removal of the axillary lymph nodes.
- 3- Lumpectomy: denotes removal of the tumor with at least 1 cm of normal breast tissue.
- 4- Simple mastectomy: removal of the breast tissue without removal of the axillary lymph nodes. <sup>(121)</sup>

#### 1-11-2 Radiotherapy:

Usually designed before surgical treatment. <sup>(122)</sup>

#### 1-11-3 Chemotherapy:

Different regimens of cytotoxicity drugs have been applied for different stages of breast cancer and in combination with surgery and radiotherapy. Drugs given include CMF (Cyclophosphamide, Methotrexates and Fluorouridine) and CA (cyclophosphamide and doxorubicine). <sup>(123)</sup>

#### 1-11-4 Hormonal therapy:

Especially useful for estrogen rich tumors, widely used anti-estrogen agent is tamoxifen in 20 mg daily dose. <sup>(124)</sup>

Recent adjuvant therapies include aromatase inhibitors as Arimidex and gene targeted therapy as Herceptin.<sup>(125)</sup>

## 1-12 Prognosis of breast cancer:

Prognosis is the ultimate outcome of the disease and is usually expressed in crude certain period survival rates and disease free survival.<sup>(126)</sup> The crude five years survival rate of the breast cancer after conventional treatment range varies between 63.5 and 32.0.<sup>(127)</sup>

The prognosis of the breast cancer is influenced by certain biological, clinical, immunological and pathological variables<sup>(128)</sup>; the main one being the pathological stage of the disease. In addition to TNM stage of BC, predictor of tumor invasiveness and metastasis include the histological type, angiogenic markers, and markers of cell proliferation.<sup>(128)</sup> While predictors of tumor growth rate are the histological grade, ER and PR receptors expression, genetic markers as HER2/ neu and EGFR expression and cell proliferation markers such as mitotic index, S- phase fraction Ki- 67 and PCNA.<sup>(128)</sup> Predictors of efficacy of response to treatment are other prognostic factors, including expression of hormone receptors and certain genes as HER2/ nue.<sup>(128)</sup>

## 1-13 Preparation of histological sections:

Histological sections taken for diagnosis of breast cancer, as other tissues, are first processed to produce slides for microscopical examination.

### Steps of routine tissue processing:

**1- Specimen accessioning:** includes specimen reception with ensuring of adequate information in the request form and labeling of both specimen containers and request form.

**2- Gross examination:** performed by a pathologist and include description of the specimen and placing all or representing parts of it in labeled cassettes.

**3- fixation:** means attempt of permanent preservation of the tissue by immersing it into a fixative substance. Fixatives are chemicals usually belonging to one of these groups: aldehydes, alcohols, mercurial, oxidative agents and picrates.

**4- Tissue processing:** aiming to make the tissue amenable for subsequent cutting by microtome. Processing include embedding of the tissue in paraffin wax, proceeded by tissue dehydration using series of alcohol dilutions , then clearing up alcohol by xylene.

**5-Sectioning:** is cutting of processed tissue by microtome into small (6-8 microns) sections.

**6- Staining** : routine staining is by using Hematoxylin and Eosin dyes. Steps of staining include removal of paraffin wax out of the tissue then stepped rehydration of the tissue using series of alcohol dilutions.

Hematoxylin is a basic dye and stains the nucleus blue; while Eosin is an acidic dye with an affinity for the cytoplasmic components of the cell. Both dyes need a mordant, usually metallic ion, for active staining.

**7- Coverslipping**: includes covering of the stained section with thin glass to protect the tissue from being scratched. First the section is dehydrated and cleared and then covered with a mounting substance.

Processing of the histological section from fixation to Coverslipping is the function of a histotechnologist, who deliver the slide to a pathologist for reading and final reporting.

## OBJECTIVES

### General objectives:

To review the clinical, pathological and epidemiological features of breast cancer in the study area.

### Specific Objectives:

- 1- To review the histological patterns of Breast Cancer among the study population.
- 2- To determine the histological grades of breast cancer according to Modified Bloom's Richardson's grading system, among the study population.
- 3- To review the clinical presenting features of breast cancer in the study population.

## PATEINTS AND METHODS

### 2.1 Study design:

The study is a descriptive retrospective recorded data -based study.

### 2.2 Study area:

The study was conducted at the National Health Laboratory (NHL), Department of Histopathology. It is the major public section lab in the country, providing nationwide diagnostic, training and research services.

### 2.3 Study population:

Cases diagnosed as breast cancer in the department of histopathology in the study area, from January 2002 up to December 2005.

### 2.4 Inclusion criteria:

Cases of breast cancer with full records and histopathological slides

### 2.5 Exclusion criteria:

Cases with deficient records (missed request forms) or missed histopathological slides.



## 2.6 Data collection:

Data were collected from the patients request forms into a pre-designed questionnaire with detailed personal, clinical and pathological data. The slides were collected and reviewed to confirm the diagnosis of breast cancer, to determine the histological type using the WHO classification of breast cancer and to grade the tumor using the modified Bloom's Richardson's grading system .

## 2.7 Data analysis and statistics:

The data were analyzed electronically using computer program SPSS version 10.

## RESULTS

The total number of patients with breast cancer during the study period was 364; 64 of them had missed slides and consequently excluded from the study. The remainders (300) patients were selected and studied.

### 1-3 Characteristics of the studied patients:

#### 1-3-1 Age distribution:

The age of the studied patients ranged from 21 years to 77 years, with a mean of  $44.5 \pm 13.7$  years. 37.3% were below the age of 40 years of age. The age group with highest frequency was (35-44) years (**Figure1**).

#### 3-1-2 Sex distribution of the patients:

Two hundred and sixty two (87.3%) of the patients were females, compared to 38 (12.7%) males (**Figure 2**). Thus, the male to female ratio was 1:6.89. IDC was diagnosed in 34 (89.5%) of the males and in 228 (87.0%) of the female. While ILC was found in only one male (2.6%) compared to ten cases in females (3.2%). Statistical analysis did not approve correlation between the gender of the patient and the histological type of the tumor (P. value .784).

48% of males underwent simple mastectomy compared with 17% of the females. On the other hand, lumpectomy was performed more in females (29% of them) than in males (8.4% of them) .This relationship was significant (P value 0.00). **(Figure 8)** illustrates the relationship between the sex of the patient and the type of operation.

### 3-1-3 Residence distribution in breast cancer:

Concerning the residence of the patients, one hundred and twenty six (42%) of them came from the central regions including Khartoum and the four central states. Eighty one (27%) patients were from the northern region. The West, the East and the South were represented with thirty (10%), twenty four (08%) and eighteen (06%) patients respectively. In twenty one patients (07% of the cases) the residency was not stated in the request form **(Figure4)**.

### 3-2 Distribution of the clinical symptoms among studied patients:

The various clinical presentations of the breast cancer in the studied group were shown in the **table (1)**. All of the patients (100%) had breast mass or lump. Come second is pain which was recorded in sixty three (21%) cases. Nipple retraction was found in thirty nine (13%) cases, while skin ulceration and weight loss were seen in twenty seven (09%) and twenty one (07%) patients

respectively. Other conditions (including the cases in which no symptom is recorded) were observed in fifty one (17%) of the cases.

### 3-3 Site distribution of the breast cancer:

**Figure (5)** demonstrates the site distribution of the breast cancer in the studied patients. Right sided and left sided cancer were found almost with equal frequencies, (42.7%) and (45.3%) respectively. The tumor was found bilateral in (3%) of the cases. Again, no information concerning the site was given in (9%) of the set up.

### 3-4 Type of operation:

Five modes of operation were used to obtain the specimen from the studied patients. The most frequently used procedure was radical mastectomy with axillary clearance (42.7%). Lumpectomy was performed in (28.3%) and simple mastectomy in (21.3%) of the cases. Quadrantectomy and core needle biopsy were both rare options (three cases for each). The type was not mentioned in (5.3%) of the cases (**Table 2**).

### 3-5 Histopathological characteristics of BC among the studied patients:

#### 3-5-1 Histological types:

The diagnosis of breast cancer in this study is based solely on the histopathological examination of the surgical specimens.

The vast majority (95.0%) were invasive tumors, while non invasive carcinoma including DCIS and LCIS constituted only (5.0%) of the cases **(Figure 7)**.

IDC was the predominant histological types; seen in (87.3%) of cases. Come second is ILC (3.7%). Ductal carcinoma in situ was diagnosed in (4.0%) of the cases. Other histological patterns include papillary carcinoma (2%), mucinous carcinoma (0.7%), lobular carcinoma in situ (1%), malignant phyllodes (0.7) % tumors and tubular carcinoma (0.7%) **(Figure 6)**

#### 3-5-2 Grading:

Modified Bloom's and Richardson's grading system was applied in this study. The majority of the cases (53.3%) were designed as grade 3 in this scale, followed by grade 2 (34%%) and lastly grade 1(12.7%) **(Table 3)**

**Table 1: Clinical presentations of breast cancer among  
the study population**

<b>Clinical presentation</b>	<b>Frequency</b>	<b>Percentage</b>
Breast lump	300	100%
Pain	63	21%
Nipple discharge	30	10%
Skin ulceration	27	9%
Nipple retraction	39	13%
Weight loss	21	7%
Others	51	17%
<b>Total</b>	<b>300</b>	<b>100.0%</b>

**Table 2: Type of operations performed to the study population**

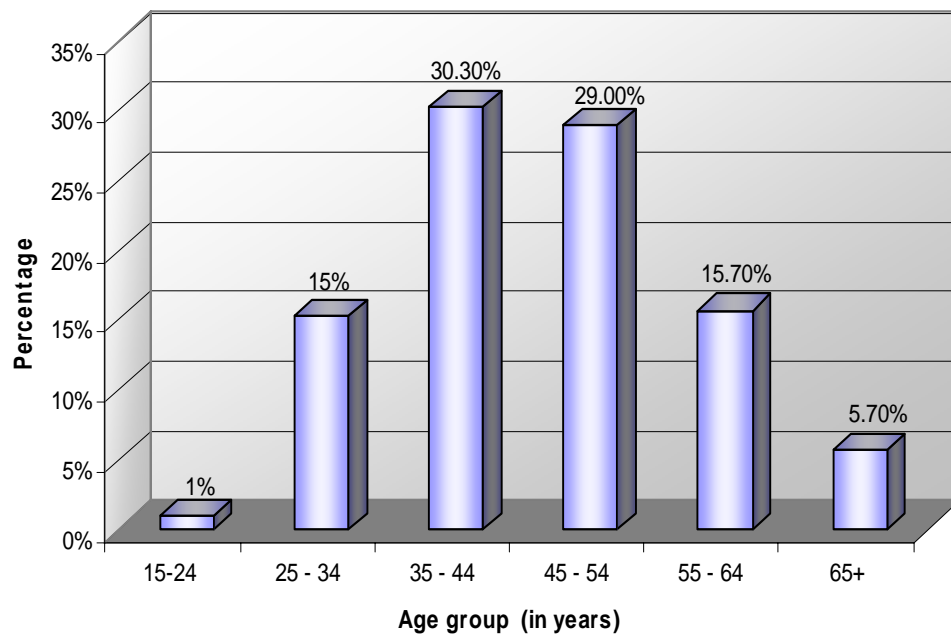
<b>Type of operation</b>	<b>Frequency</b>	<b>Percentage</b>
Mastectomy plus axillary clearance	128	42.7%
Simple mastectomy	64	21.3%
Lumpectomy	85	28.3%
Quadrantectomy	3	1.0%
Core biopsy	3	1.0%
Not stated	17	5.7%
<b>Total</b>	<b>300</b>	<b>100.0%</b>

**Table 3: Grading scores for breast cancer among  
the study population**

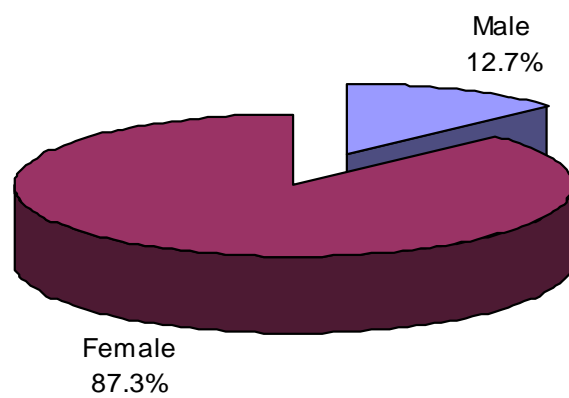
<b>Grade</b>	<b>Frequency</b>	<b>Percentage</b>
I	38	12.7%
II	102	34%
III	160	53.3%
<b>Total</b>	<b>300</b>	<b>100.0%</b>

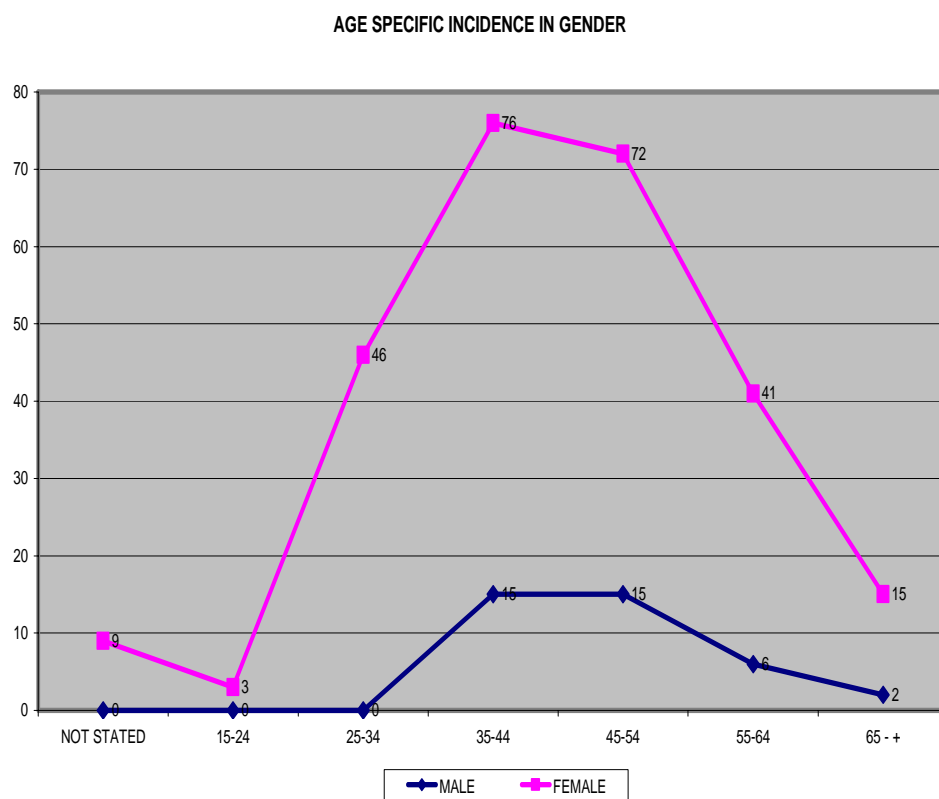


**Fig. 1: Age distribution of the study population**



**Fig. 2: Sex distribution of the study population**

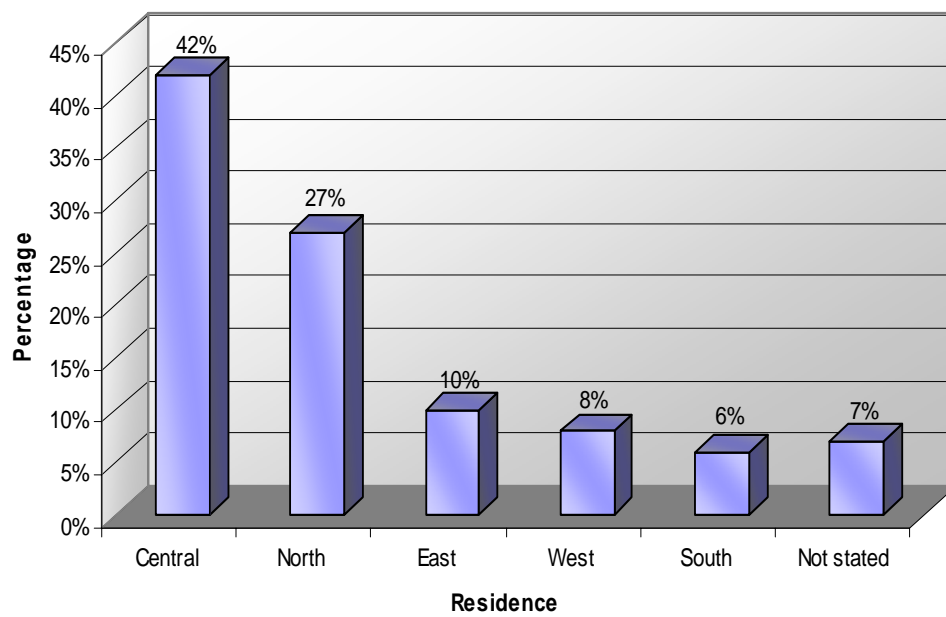




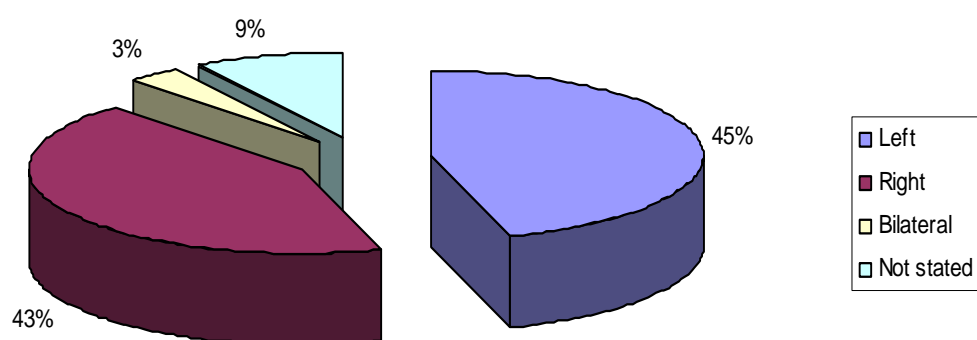
**Figure (3): Age specific incidence rate of BC in males and females among the study group**

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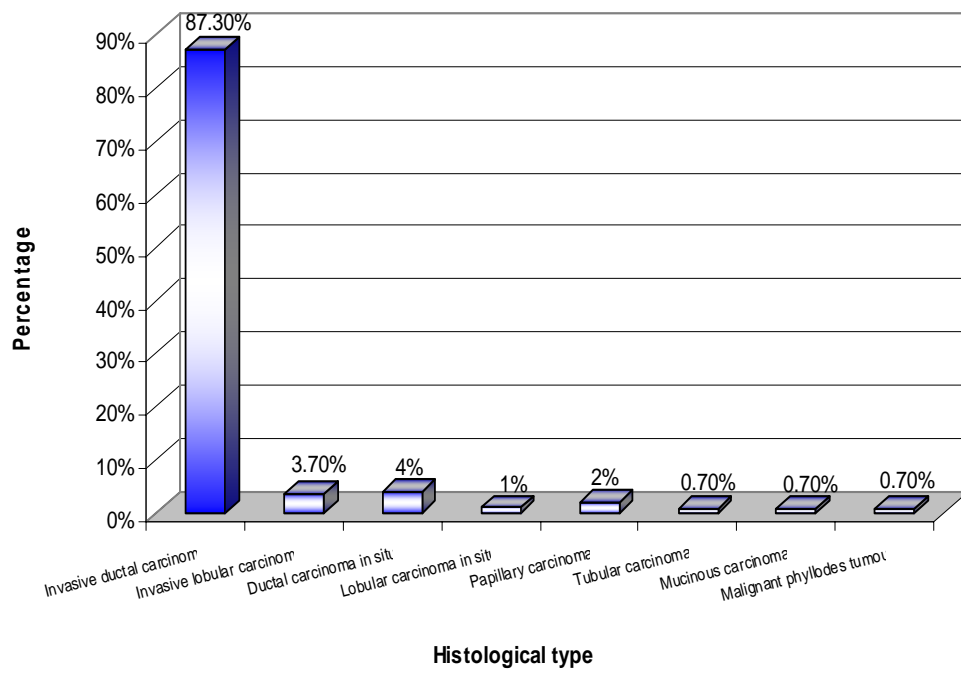
**Fig. 4: Distribution of the study population according to residence**



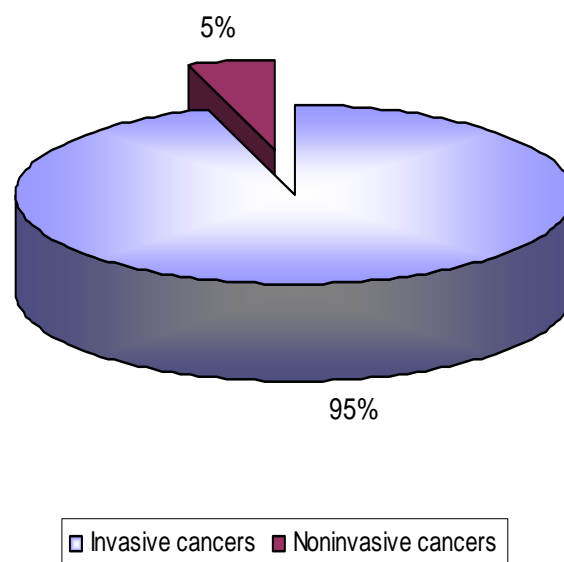
**Fig. 5: Site distribution of breast cancer among the study population**

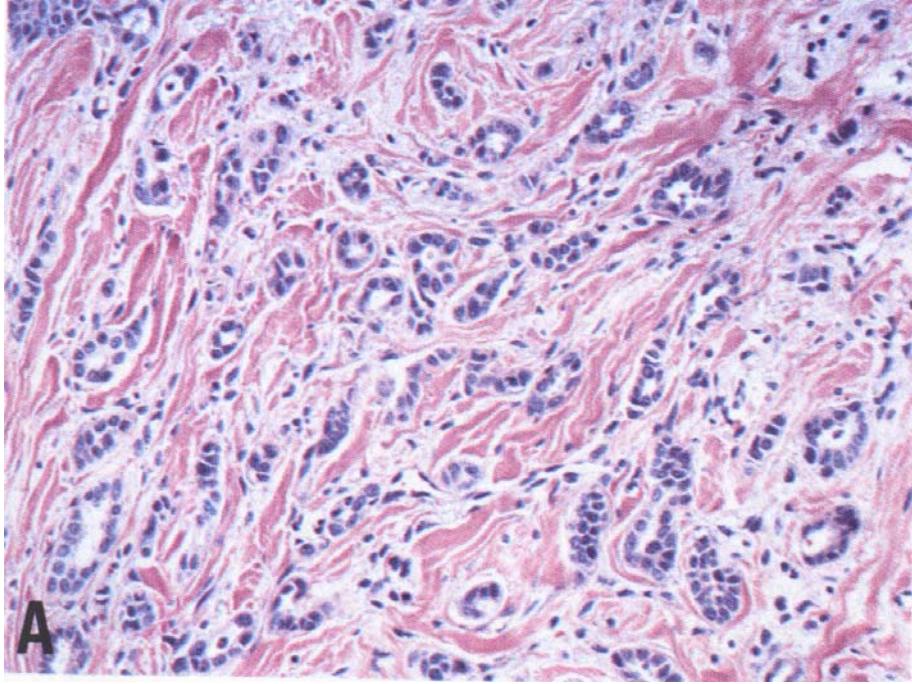


**Fig. 6: Histological types of breast cancer among the study population**



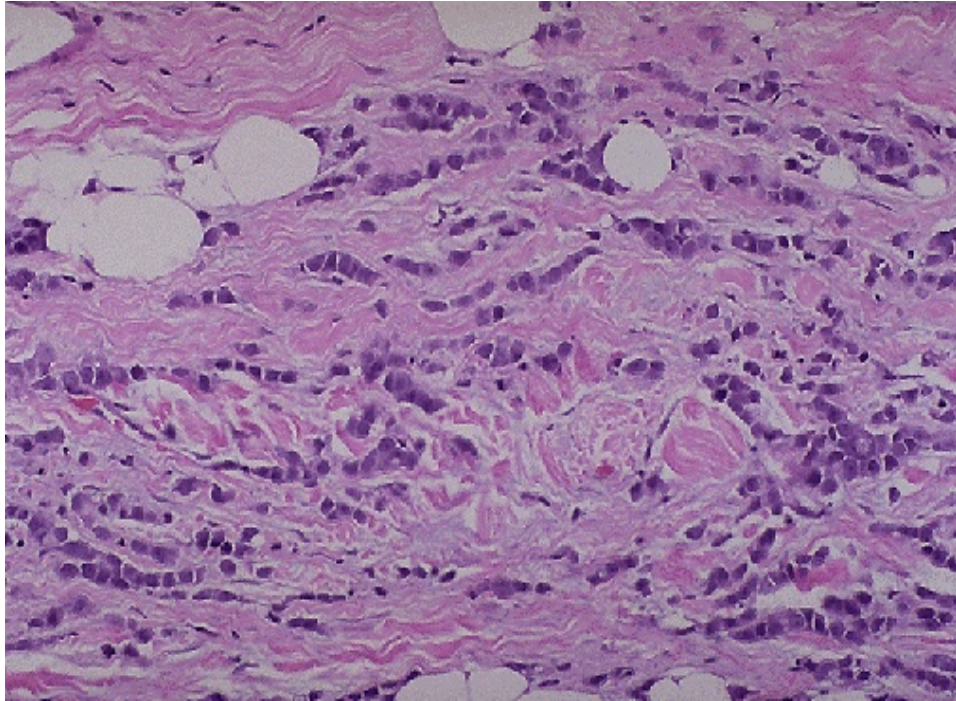
**Fig. 7: Frequencies of invasive and non-invasive cancers among the study population**



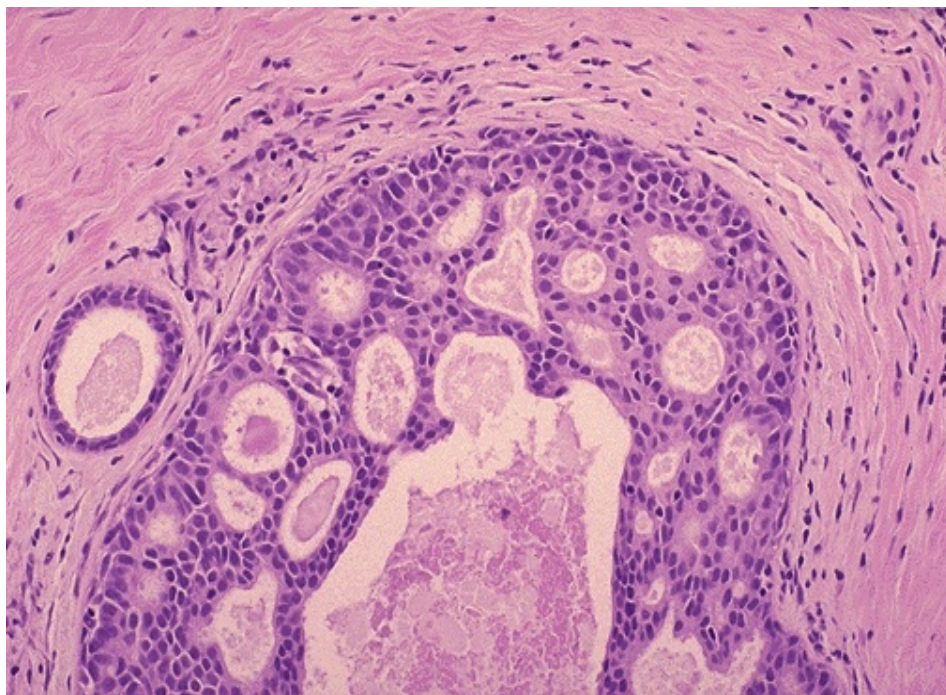


**Figure(9) Invasive ductal carcinoma .Tubular formation  
Grade 1(H&E X 40)**

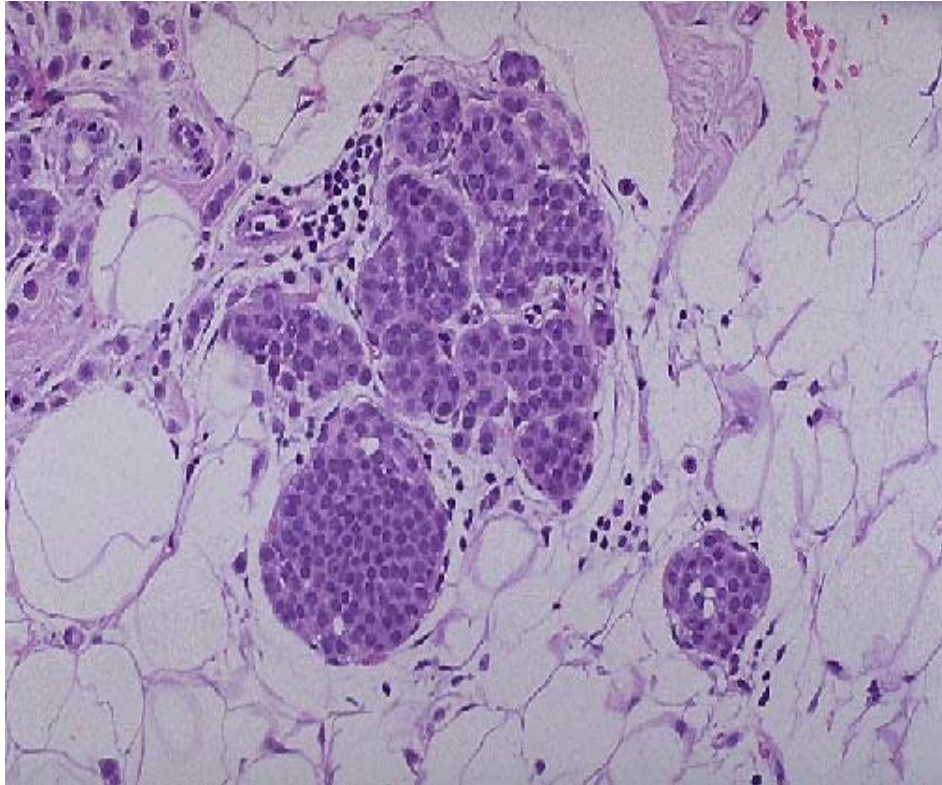




**Figure(10) Invasive lobular carcinoma, Indian file pattern.  
(H&E X 40)**

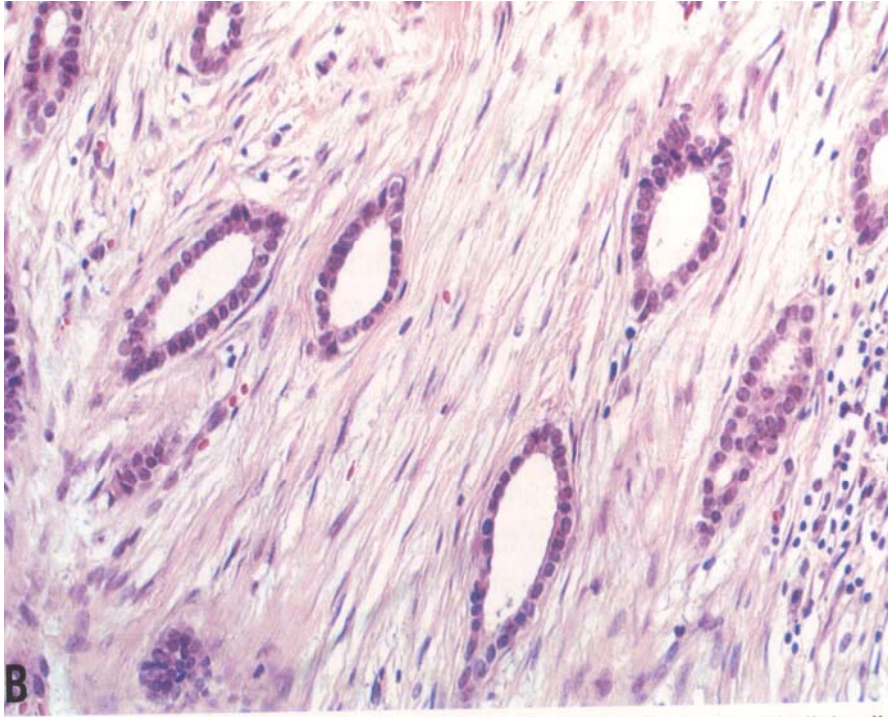


**Figure (11): Ductal carcinoma in situ(DCIS) Cribriform pattern  
(H&E X 40)**

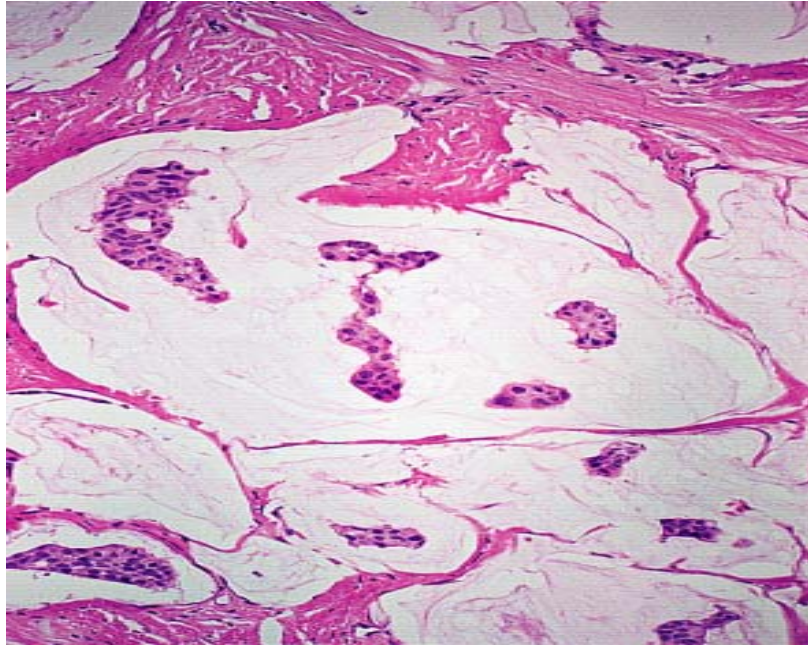


**Figure (12) Lobular carcinoma in situ  
(H&E X40)**

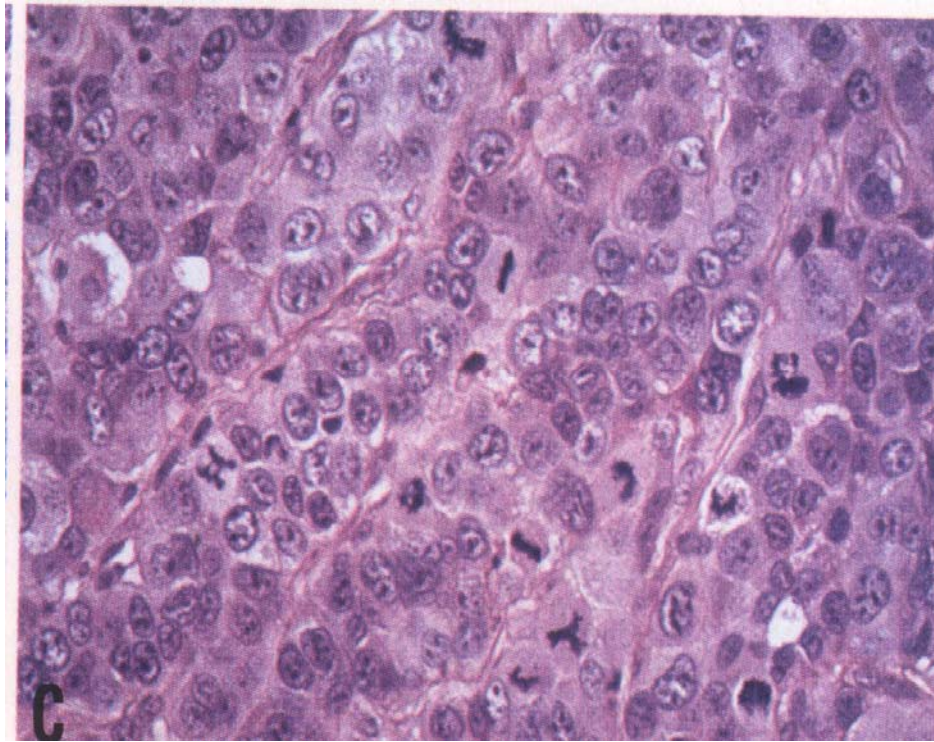




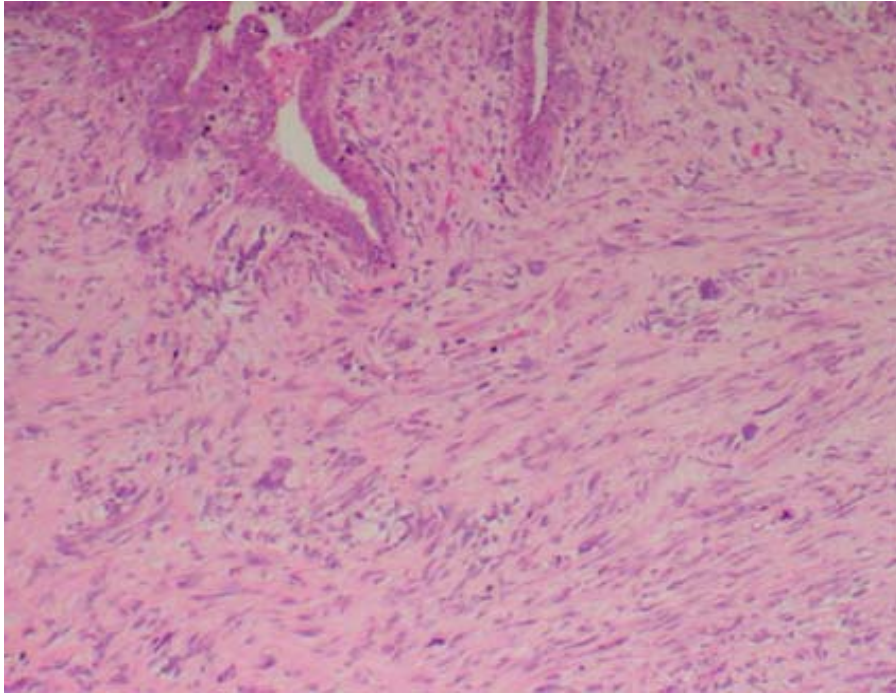
**Figure (13) Tubular carcinoma  
(H&E X40)**



**Figure(14) Mucinous carcinoma of the breast  
(H&E X 40)**



**Figure (15) Invasive ductal carcinoma: mitotic figures.  
(H&E X 60)**



**Figure (16) Malignant phyllodes tumor  
H&E (X40)**

## DISCUSSION

This study is a retrospective descriptive one addressed to the breast cancer in Sudanese patients. It was carried out in the period from January 2002 to December 2005 and includes analysis of 300 cases.

The epidemiological, clinical and pathological characteristics of breast cancer has been an area of great interest to many researchers especially in Africa and the developing countries where it has been scoring rising incidences, despite the fact that it is lower than in more affluent societies. <sup>(5)</sup>

In our country, there has been significant increase in all cancers incidences, the leading one being breast cancer, which reached alarming levels during the last decade. <sup>(4)</sup> This can be attributed, at least in part, to the trends in the Sudanese society towards urbanization and socioeconomic advances, which are linked to predisposition to this disease . In addition, increased medical awareness among people rendered them more readily seek advice and thence increased discovered cases. However, up to now there is no satisfactory and reliable data on the absolute cancer rates in Sudan.



This study encountered many difficulties and limitations due to the quality of the registered data on which the study was based, in particular the undetailed history and the clinical information necessary to assess the stage of the cancer. So caution should be taken when the results are interpreted with the international data.

In regard to sex distribution of the breast cancer, the results of this study can be read with those carried out in Africa sub-Saharan countries, with higher proportion of BC among males than in the global ratio<sup>(3,16,42)</sup> However, female predominance is still the rule, with females figure of (87.3 %) and males (21.7 %). This can easily be explained on the back ground of the anatomical and physiological genders differences entailed in the pathogenesis of this cancer.<sup>(21, 24)</sup> Statistical analysis showed significant influence of the sex on the type of operations. But there was no relation between the genders of the patients and the histological type, in contrast to the general believes that lobular carcinoma tends to predelicate to males.<sup>(9)</sup>

In this study the mean age of the patients was found to be  $44.5 \pm 13$  years. This is not much different from the mean age of BC in many Arab countries<sup>(117)</sup> and Sub Saharan African countries<sup>(42)</sup> It is more than twelve years younger than the age of 57 years

currently accepted for the Western communities. <sup>(15, 44)</sup> In addition, BC was found more frequent in the age group (35-44). Furthermore, (37.3%) of the patients in our set up were below the age of 40 years. This observation should alert the clinicians in our country to be more cautious in managing breast lumps especially in the younger age groups.

Regarding the residency distribution, the majority (42%) of the patients came from the central regions (including the capital Khartoum and the four central states), the least frequent place of origin being the most remote states. This can readily be explained on the basis of the demographic and economic characteristics of the Sudanese population, in that most of the Sudanese are clustered in the big towns and also the unjustified focusing of the medical service in the capital. In addition, many people particularly in the rural areas fail to reach hospitals for diagnosis and treatment, not only because of lack of transport, but also due to their poor socioeconomic status and prevalence of some taboos as reliance and believes on herbal and spiritual medicine. However, the detailed social history was omitted from the records in most cases so was not analysed.

Special attention should be paid to the disproportional high rate of BC in the patients from the North (27%). Further

demographical and environmental studies are highly recommended in that part of the country.

In this study, the results are in agreement with the literature regarding the occurrence of BC in almost equal rates in right (42.7%) and left(45.3%) breast<sup>(6)</sup>. Bilateral BC was recorded in only (3%) of the patients.

The present study found that all (100%) of the cases had at least one symptom at the time of diagnosis. Absence (00%) of asymptomatic BC patient highlights the negligibility of the role of cancer screening program, if any, in contrast to the situation in the developed countries. <sup>(87, 90)</sup>

Moreover, higher proportions than what is internationally accepted of patients presented with signs of advanced BC such as skin ulcerations (09%) and nipple changes (13%). This may be due to social and cultural factors. Sudanese females are usually too reluctant to report small breast lumps for clinical examination. Again, this indicates that any effective future screening program is likely to improve dramatically the dim picture imposed by this dreadful dilemma.

The most frequent (43%) type of operation in our set up was radical mastectomy with axillary clearance, with higher proportion of this option among the elder age groups (86% in patients above sixty compared to 20% in patient under thirty five years). Conservative surgery tends to be done in younger age groups. For instance, lumpectomy was performed in 39% of patient under thirty five in contrasts to only 6% in patients above sixty five years. Statistical analysis proved this relationship between the age of the patient and the mode of surgical therapy (P value 0.00).Core biopsy was done in Only 6 patients (2%). This is apparently due to the fact that it is only a diagnostic procedure in contrasts to the other options which are mainly therapeutic.

On the view of the limitations of this study, only eight histological types of BC were encountered in the studied population. The vast majority (87%) was diagnosed as IDC. This result generally agrees with many literature values in the developing countries. <sup>(117,</sup>  
<sup>3)</sup> Invasive lobular carcinoma was seen in (3.7%) of the cases. Non invasive cancers (DCIS & LCIS) in this study showed markedly lower frequency (5%) in comparison to the western population. Again, screening may play a role in this point. Other histological types are all rare and include papillary carcinoma(2.0%),tubular carcinoma

(0.7%), mucinous carcinoma (0.7%) and malignant phyllodes tumor (0.7%). In general, the histological types had no specific predilection for any age group (P. value 0.848) or gender (P. value 0.783) .

Most of the patients in this study (51%) were assigned as high grade carcinoma (grade 3 in modified Bloom's and Richardson's system), further highlighting the aggressive nature of BC, in view that many patients came at later clinical stage of the tumor judged by tumor size, involvement of the lymph nodes and systemic metastasis. Unfortunately, our study could not assess the later important parameters due to intractable deficiency in the recorded data.

So further work is needed to shed more light on the natural history of breast carcinoma in Sudanese patients and probably a collaborative multicenter study which includes all oncological centers in the county can fulfill this goal.

## CONCLUTION

- Regardless the limitations of this study, it indicated that our country shares many BC clinical and pathological characteristics in common with other developing countries and in contrasts to the western or developed countries.
- These characteristics include the trend toward a greater incidence in younger age groups, a higher male- female ratio and higher frequencies of clinical and pathological indicators of more aggressiveness of the tumor.
- The study identified only eight histological types of BC, namely: ICD, ILC, DCIS, LCIS, medullary carcinoma, papillary carcinoma, mucinous carcinoma and malignant phyllodes tumors.

## RECOMMENDATIONS

- Further in- depth studies are highly recommended to be carried out for more evaluation of risk factors and to find out the cause of high rates of the disease in this country, especially the Central and Northern regions.
- Implementation and community promotion of breast cancer screening program for early detection and better prognosis.
- Establishment of specialized breast centers and clinics to improve the screening, diagnosis and treatment services.
- Improvement of cancer reporting and registration activities.

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